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FACING ELDERLY RECIPIENTS IN COMBINED LIVER-KIDNEY TRANSPLANTATION

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ABBREVIATIONS

CIT = cold ischemia time

CLKT = combined liver-kidney transplantation

DCD = donation after circulatory death

DGF = delayed graft function

ECD = extended criteria donor

GFR = glomerular filtration rate

KT = kidney transplantation

LT = liver transplantation

MELD = model for end-stage liver disease

UNOS = United Network for Organ Sharing

Aging is an unavoidable process we all face. In the United States, according to the census.gov, the highest projected increase in population will be seen in age groups (i) ≥85 years (42% increase by 2030 and 191% by 2050) and (ii) ≥65 years (48% increase by 2030 and 74% by 2050)[1]. Therefore, we, transplant physicians, will have to deal with more elderly donors and recipients. This fact has already been confirmed by the Scientific Registry of Transplant Recipients (SRTR). Table 1 summarizes the SRTR data on liver transplant recipients who were ≥65 years old, comparing the year-end in 2007 and 2017[2]. Absolute number of recipients who were 65 years or older undergoing liver transplant increased by 250% from 2007 to 2017 and it is expected to increase more in upcoming years[2].

Another important physiological reality with aging is that elderly population may have higher susceptibility to chronic kidney disease (CKD) due to the known fact of reduced number of nephrons and glomerular filtration rate. Thus, more elderly patients will be candidates for combined liver-kidney transplantation (CLKT, simultaneous liver-kidney transplantation). However, elderly recipients may carry a higher risk when it comes to the CLKT due to the magnitude of operation and higher chances of delayed graft function (DGF) of the transplanted kidney, which significantly correlates with patient's mortality[3,4]. Debates have been ongoing on the determination of age cutoff for CLKT whether elderly recipients (≥65 years), especially those 70 years and older, should be considered for transplantation.

In this issue of Transplantation, Goldberg et al.[5] reported a detailed analysis of the SRTR data between 2002-2018 with a total cohort of 3146 CLKTs with CKD, of which 465 (14.8%) were 65-69 years, and 93 (3.0%) were ≥70 years. They sought to answer a question whether there was an appropriate age cutoff for a CLKT in elderly patient with CKD. They found that compared to recipients aged 50-64 years, the most notable differences among CLKT recipients with CKD 65-

69 and ≥70 years of age were (i) more likely to be of white race, (ii) have NASH/cryptogenic cirrhosis, (iii) received higher KDPI 'worst' kidneys, (iv) have higher percentage of diabetes, especially in age group ≥70 years, and (v) less likely to be on dialysis before transplant. Goldberg et al. also reported that the unadjusted 5-year survival of CLKT recipients ≥70 years of age with CKD was 58% as compared to 69% in CLKT recipients ≥70 years of age without CKD, and both were lower compared to other age groups, such as 40-49, 50-59, 60-64, and 65-69 years of age[5]. Although there were some CLKT recipients without CKD which is controversial in many jurisdictions around the world, the SRTR data spanned between 2002-2018. They also highlighted that kidney DGF was a statistically significant variable for patient survival.

Similar to Goldberg et al.[5], Croome et al.[6] analyzed the SRTR database including all adult CLKTs without any definition of CKD (a cohort of 5194 patients). Croome et al came up with a scoring system based on multivariate analysis outcomes, which indicated (i) MELD score (per 5 points increments), (ii) recipient age ≥70 years, and (iii) being on the ventilator at the time of CLKT negatively impacted the patient survival[6]. In fact, the authors stated that using "the scoring system", CLKT should be avoided in patients ≥65 years of age on mechanical ventilation prior to CLKT, and in patients ≥70 years of age with a MELD score ≥30[6]. However, Croome et al reported that similar patient and graft survival were observed in CLKT recipients aged ≥65 years compared to CLKT recipients aged <65 years, as well as liver transplant alone recipients aged ≥65 years[6]. At Indiana University, we have confirmed the same outcome[7], as Croome et al.[6] that there was no difference in patient survival in CLKT recipients aged 18-45, 46-64, or ≥65 years. However, when we further analyzed the impact of recipient age (18-45, 46-59, 60-69, and ≥70 years) in CLKT, we found that those aged ≥70 years had significantly lower patient survival[7]. Although the percentage of CLKT recipients aged ≥70 years was 8% at Indiana

University compared to 2.6[7]–3%[6] in SRTR, the absolute number was only 8 recipients, which could be a limiting factor due to single-center analysis and small numbers in each cohort[7]. Therefore, the recent report from Goldberg et al.[5] is important to increase the statistical power with detailed analyses of CLKT recipients ≥70 years of age.

In CLKT, different approaches have been implemented with the effort of ameliorating the donor and recipient variables in order to provide better outcomes despite the use more marginal donors. One of the most notable approaches is the Indiana Approach where the kidney portion of the CLKT is delayed up to 2-3 days while kidneys are pumped continuously[3,7-10]. The Indiana Approach in CLKT offers a less hostile environment with hemodynamically more stable patient (possibly without any vasopressor support) at the time of kidney transplantation[3,7-9]. Hemodynamically stable liver transplant recipient means that the risk for kidney DGF would be minimized. Kidney DGF, as the negative factor on patient survival in CLKT recipients, was previously highlighted by single-center analyses by Ekser et al.[3], and Lunsford et al.[10], and most recently by the SRTR analysis by Weeks et al.[4].

Therefore, putting together from various studies in CLKT analyzing elderly recipients[3,5-7], several considerations should be remembered; (i) elderly patients ≥65 years of age on a mechanical ventilation prior to CLKT, and patients ≥70 years of age with a MELD score ≥30 need particular attention with multiple considerations, (ii) DGF should be avoided in any CLKT recipient, particularly in elderly recipients, (iii) better quality kidneys (per KDPI) should be considered when transplanting elderly recipients in CLKT.

The aging is inevitable[1] and we (will) transplant more elderly recipient is the fact[2]. Therefore, we should find the ways to improve our approaches and outcomes in order to prepare ourselves and patients to the next level.

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Table 1: Scientific Registry of Transplant Recipients (SRTR) data.

	2007	2017	Percentage Increase
Total Number of Liver Transplant Recipients ≥65 years old	648	1674	258%
Percentage of Liver Transplant Recipients ≥65 years old in All Adult Liver Transplant Recipients	11%	22.4%	100%